A fifth group turns skin to neurons, creating a model for Alzheimer's disease

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A few weeks ago, my colleague used this space to discuss the second and third papers showing teams had turned skin cells directly into neurons, noting that this replication of research results is essential to verifying the initial breakthrough while refining and improving it. She noted that only after much replication and refinement would she or anyone else want the resulting cells for therapy. Since then a fourth team reported another technique and now a fifth group is reporting the more likely short term benefit-a disease in a dish model for a neurodegenerative disease.

The first two papers came from work in the CIRM funded facility at Stanford University. The breakthrough paper in May from Marius Wernig reported a slow and inefficient process for using certain factors to directly reprogram skin cells into nerve cells without first taking them through an embryonic-like state. The follow-up paper in late July came from Stanford colleague Gerald Crabtree and showed marked improvement in efficiency and the nerve-like functioning of the cells. That same week at team from Milan reported another efficient system for creating nerve cells but this time directing them to become dopamine-producing cells like those lost in Parkinson's disease. And last week at team at the Gladstone Institutes in San Francisco, using another CIRM funded facility, reported yet another technic that also improved efficiency.

Now, a team at Columbia reported in today's issue of the journal Cell that they had developed a fifth way to accomplish this direct conversion of skin to nerve, and had done so with both skin from normal subjects and skin from patients with the inherited form of Alzheimer's disease. In both cases the cells matured and behaved like neurons, responding to neurotransmitters by letting ions like sodium and potassium cross the cell membrane. However, the cells derived form patients were also clearly abnormal. They had altered ability to process and transport the amyloid precursor protein (APP) and a resulting increase in production of amyloid beta, which has long been a suspect in the disease, but depending on what year you look at the literature, it is theorized to be a culprit or an artifact. This disease in a dish model may help to answer that question.

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Tags: crabtree, Wernig, Stanford University